

Declaration, Petition and Power of Attorney For Patent Application

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

**CTLA4-IMMUNOGLOBULIN FUSION PROTEINS HAVING
MODIFIED EFFECTOR FUNCTIONS AND USES THEREFOR**

the specification of which

(check one)

 is attached hereto.

X was filed on February 2, 1996 as

Application Serial No. 08/595,590

and was amended on _____
(if applicable)

I do not know and do not believe that the subject matter of this application was ever known or used in the United States before my invention thereof or patented or described in any printed publication in any country before my invention thereof or more than one year prior to the date of this application; and that said subject matter has not been patented or made the subject of an issued inventor's certificate in any country foreign to the United States on an application filed by me or my legal representatives or assigns more than twelve months prior to the date of this application; that I acknowledge my duty to disclose information of which I am aware which is material to the examination of this application, that no application for patent or inventor's certificate on the subject matter of this application has been filed by me or my representatives or assigns in any country foreign to the United States, except those identified below, and that I have reviewed and understand the contents of the specification, including the claims as amended by any amendment referred to herein.

I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

10027075-1-122001

PRIORITY CLAIM

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed.

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CLAIM FOR BENEFIT OF EARLIER U.S./PCT APPLICATION(S)

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Send Correspondence to:

Amy E. Mandragouras, Esq., Lahive & Cockfield, 60 State Street, Boston, MA 02109

Direct Telephone Calls to: (name and telephone number)

Amy E. Mandragouras, Esq. (617) 227-7400

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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Inventor's signature	Date
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Inventor's signature	Date
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Citizenship United States of America	
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Full name of third inventor Kashi Javaherian	
Inventor's signature	Date
Residence 27 Webster Road, Lexington, MA 02173	
Citizenship	
Post Office Address (if different)	

Full name of fourth inventor Cindy L. Jellis	
Inventor's signature	Date 3/1/11
Residence 3 Brian Drive Londonderry, New Hampshire -03053	
Citizenship United States of America	
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Full name of fifth inventor Paul D. Rennert	
Inventor's signature	Date
Residence 2 Sky View Terrace, Holliston, Massachusetts 01746	
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Full name of sixth inventor Sandra Silver	
Inventor's signature	Date
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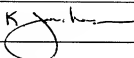
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Inventor's signature 	Date 6/4/96
Residence 27 Webster Road, Lexington, MA 02173	
Citizenship USA	
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Inventor's signature	Date
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Post Office Address (if different)	

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Full name of second inventor Jerry Carson	
Inventor's signature <i>Jerry Carson</i>	Date <i>May 21, 1986</i>
Residence 2 Kent Street, Belmont, Massachusetts 02178	
Citizenship United States of America	
Post Office Address (if different)	

Full name of third inventor Kashi Javaherian	
Inventor's signature	Date
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Direct Telephone Calls to: (name and telephone number)

Amy E. Mandragouras, Esq. (617) 227-7400

Wherefore I petition that letters patent be granted to me for the invention or discovery described and claimed in the attached specification and claims, and hereby subscribe my name to said specification and claims and to the foregoing declaration, power of attorney, and this petition.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of first inventor Gary S. Gray	
Inventor's signature	Date
Residence 32 Milton Road, Brookline, Massachusetts 02146	
Citizenship United States of America	
Post Office Address (if different)	

Full name of second inventor Jerry Carson	
Inventor's signature	Date
Residence 2 Kent Street, Belmont, Massachusetts 02178	
Citizenship United States of America	
Post Office Address (if different)	

Full name of third inventor Kashi Javaherian	
Inventor's signature	Date
Residence 27 Webster Road, Lexington, MA 02173	
Citizenship	
Post Office Address (if different)	

Full name of fourth inventor Cindy L. Jellis	
Inventor's signature	Date
Residence 3 Brian Drive, Londonderry, New Hampshire 03053	
Citizenship United States of America	
Post Office Address (if different)	

Full name of fifth inventor Paul D. Rennert	
Inventor's signature	Date
Residence 2 Sky View Terrace, Holliston, Massachusetts 01746	
Citizenship United States of America	
Post Office Address (if different)	

Full name of sixth inventor Sandra Silver	
Inventor's signature <i>Sandra Silver</i>	Date <i>May 16, 1996</i>
Residence 350 Marlborough Street, Boston, Massachusetts 02115	
Citizenship United States of America	
Post Office Address (if different)	

10027075-122001

Declaration, Petition and Power of Attorney For Patent Application

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

**CTLA4-IMMUNOGLOBULIN FUSION PROTEINS HAVING
MODIFIED EFFECTOR FUNCTIONS AND USES THEREFOR**

the specification of which

(check one)

☐ is attached hereto.

☒ was filed on February 2, 1996 as

Application Serial No. 08/595,590

and was amended on _____
(if applicable)

I do not know and do not believe that the subject matter of this application was ever known or used in the United States before my invention thereof or patented or described in any printed publication in any country before my invention thereof or more than one year prior to the date of this application, and that said subject matter has not been patented or made the subject of an issued inventor's certificate in any country foreign to the United States on an application filed by me or my legal representatives or assigns more than twelve months prior to the date of this application; that I acknowledge my duty to disclose information of which I am aware which is material to the examination of this application, that no application for patent or inventor's certificate on the subject matter of this application has been filed by me or my representatives or assigns in any country foreign to the United States, except those identified below, and that I have reviewed and understand the contents of the specification, including the claims as amended by any amendment referred to herein.

I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

10027075.122001

PRIORITY CLAIM

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed.

Check one:

☒ no such applications have been filed.

☐ such applications have been filed as follows

EARLIEST FOREIGN APPLICATION(S), IF ANY FILED WITHIN 12 MONTHS
(6 MONTHS FOR DESIGN) PRIOR TO THIS U.S. APPLICATION

Country	Application Number	Date of Filing (month,day,year)	Priority Claimed Under 35 USC 119
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No

ALL FOREIGN APPLICATION(S), IF ANY FILED MORE THAN 12 MONTHS
(6 MONTHS FOR DESIGN) PRIOR TO THIS U.S. APPLICATION

CLAIM FOR BENEFIT OF EARLIER U.S./PCT APPLICATION(S)

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application. As to subject matter of this application which is common to my earlier United States application, if any, described below, I do not believe that the same was ever known or used in the United States before my invention thereof or patented or described in any printed publication in any country before my invention thereof or more than one year prior to said earlier application, or in public use or on sale in the United States more than one year prior to said earlier application, that the said common subject matter has not been patented or made the subject of an inventor's certificate issued before the date of said earlier application in any country foreign to the United States on an application, filed by me or my legal representatives or assigns more than twelve months prior to said application and that no application for patent or inventor's certificate on said subject matter has been filed by me or my representatives or assigns in any country foreign to the United States except those identified herein.

(Application Serial No.)

(Filing Date)

(Status)
(patented,pending,aband.)

(Application Serial No.)

(Filing Date)

(Status)
(patented,pending,aband.)

10027075-122001

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorneys and/or agents to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

John A. Lahive, Jr.	Reg. No. 19,788	Jeremiah Lynch	Reg. No. 17,425
W. Hugo Liepmann	Reg. No. 20,407	Amy E. Mandragouras	Reg. No. 36,207
James E. Cockfield	Reg. No. 19,162	Elizabeth A. Hanley	Reg. No. 33,505
Thomas V. Smurzynski	Reg. No. 24,798	Matthew P. Vincent	Reg. No. 36,709
Ralph A. Loren	Reg. No. 29,325	Paul Louis Myers	Reg. No. 35,965
Thomas J. Engellenner	Reg. No. 28,711	Beth E. Arnold	Reg. No. 35,430
William C. Geary III	Reg. No. 31,359	Anthony A. Laurentano	Reg. No. 38,220
Giulio A. DeConti, Jr.	Reg. No. 31,503	Jane E. Remillard	Reg. No. 38,872
Michael I. Falkoff	Reg. No. 30,833	Jean M. Silveri	Reg. No. 39,030
Ann Lamport Hammitte	Reg. No. 34,858	Mark A. Kurisko	Reg. No. 38,944
John V. Bianco	Reg. No. 36,748	Edward J. Kelly	Reg. No. 38,936

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Full name of first inventor Gary S. Gray	
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Post Office Address (if different)	

Full name of fifth inventor Paul D. Rennert	
Inventor's signature <i>Paul D. Rennert</i>	Date 9 MAY 1996
Residence 2 Sky View Terrace, Holliston, Massachusetts 01746	
Citizenship United States of America	
Post Office Address (if different)	

Full name of sixth inventor Sandra Silver	
Inventor's signature	Date
Residence 350 Marlborough Street, Boston, Massachusetts 02115	
Citizenship United States of America	
Post Office Address (if different)	

10022152022001

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the specification of which

(check one)

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and was amended on _____
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10027075-122001

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			<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No

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10027075-122001

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(Application Serial No.)

(Filing Date)

(Status)
(patented,pending,aband.)

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Michael I. Falkoff	Reg. No. 30,833	Jean M. Silveri	Reg. No. 39,030
Ann Lamport Hammitte	Reg. No. 34,858	Mark A. Kurisko	Reg. No. 38,944
John V. Bianco	Reg. No. 36,748	Edward J. Kelly	Reg. No. 38,936

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Amy E. Mandragouras, Esq. (617) 227-7400

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Full name of first inventor Gary S. Gray	
Inventor's signature <i>Gary S. Gray</i>	Date <i>May 7, 1996</i>
Residence 32 Milton Road, Brookline, Massachusetts 02146	
Citizenship United States of America	
Post Office Address (if different)	

10027075-122001

Full name of second inventor Jerry Carson	
Inventor's signature	Date
Residence 2 Kent Street, Belmont, Massachusetts 02178	
Citizenship United States of America	
Post Office Address (if different)	

Full name of third inventor Kashi Javaherian	
Inventor's signature	Date
Residence 27 Webster Road, Lexington, MA 02173	
Citizenship	
Post Office Address (if different)	

Full name of fourth inventor Cindy L. Jellis	
Inventor's signature	Date
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Full name of fifth inventor Paul D. Rennert	
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Residence 2 Sky View Terrace, Holliston, Massachusetts 01746	
Citizenship United States of America	
Post Office Address (if different)	

Full name of sixth inventor Sandra Silver	
Inventor's signature	Date
Residence 350 Marlborough Street, Boston, Massachusetts 02115	
Citizenship United States of America	
Post Office Address (if different)	

10027075.122001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Gary S. Gray, Jerry Carson,
Kashi Javaherian, Paul D. Rennert and Sandra Silver

Continuation of
Serial No.: 09/227,595

Filed: January 8, 1999 *December 20, 2007*

For: CTLA4-Cγ4 Fusion Proteins (as amended)

Attorney Docket No.: RPN-001

Group Art Unit: 1642

Examiner: Helms, L.

Assistant Commissioner for Patents
Washington, D.C. 20231

under 1-10
Certificate of First Class Mailing (37 CFR 1.8(a))

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, *Box Patent Applications*, Washington, D.C. 20231 on the date set forth below.

December 20, 2007
Date of Signature and of Mail Deposit

By:

Larry Taylor
Megan E. Williams *Larry Taylor*
Registration No. 43,270
Attorney for Applicants

Mailing Label No. EL 8333/5914US

DECLARATION UNDER 37 C.F.R. 1.131 BY

GARY S. GRAY, JERRY CARSON, KASHI JAVAHERIAN, PAUL D. RENNERT
AND SANDRA SILVER

Sir:

We, Gary S. Gray, Jerry Carson, Kashi Javaherian, Paul D. Rennert And Sandra

Silver declare:

1. We are the inventors of the subject matter described and claimed in the above-referenced patent application.

2. Prior to July 11, 1994, the invention described and claimed in the above-referenced application was completed in this country, as evidenced by the following:

- A. Prior to July 11, 1994, we were in possession of a cloned CTLA4Ig molecule which was producing large amounts of active protein in CHO DG44 cells.

Page A-1 of Appendix A describes amino acid modifications to the Ig portion of the CTLA4Ig molecule. Deletion of the CH₂ domain from γ 1 and mutations to amino acids 235 and 237 in γ 4 are described.

Page A-2 of Appendix A describes amplification of the mutated γ 4 Hinge-CH₂-CH₃ region and the cloning of the mutated γ 4 into pNRDSH/hCTLA4 to replace the existing γ 1 Hinge-CH₂-CH₃.

Page A-3 of Appendix A describes a second method which involves the use of nested PCR to generate a mutated γ 1 (having an L to A substitution at amino acid 234, an L to E substitution at amino acid 235, and a G to A change at amino acid 237) from hCTLA4Ig and the cloning of the mutated γ 1 back into hCTLA4 pNRDSH.

Pages A-5 and A-6 show primers for use in making mutated forms of CTLA4Ig.

The notebook pages submitted as pages A-1 through A-7 of Appendix A demonstrate that we completed the claimed invention in this country prior to July 11, 1994.

- B. In addition, as shown on page A-8 of Appendix A, prior to July 11, 1994, we demonstrated that mutated forms of CTLA4Ig effectively competed with biotinylated CTLA4-Ig for binding to B7. In the experiment presented at the bottom of the page B7Ig was put onto plates. Biotinylated CTLA4Ig was added to the plates in a fixed amount. Test forms of CTLA4Ig were added in serial dilutions to test for their ability to compete for binding to B7 on the plate. In this type of assay as the amount of an effective competitor is increased, the amount of biotinylated CTLA4Ig that binds decreases. This leads to a decrease in the optical density readout. Unlabelled CTLA4Ig (left row) was used as a positive control. The data show that samples #2, #3, and #4 (in rows 2, 4, and 5, respectively) effectively competed with unmodified CTLA4Ig for binding to B7. As indicated in the table in the middle of the page, sample 2 was oncoCTLA4-m γ 4; sample 3 was IgLCTLA4- γ 1; and sample 4 was IgLCTLA4- γ 1.

10027075-122001

These data demonstrate that the modified CTLA4Ig molecules were still able to bind to B7.

Each of the dates deleted from pages A-1 through A-8 of Appendix A are prior to July 11, 1994.

We have been warned that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 or the United States Code, and that such willful and false statements may jeopardize the validity of the subject application or any patent resulting therefrom, and declare that all statements made of our own knowledge are true and that all statements made on information and belief are believed to be true.

Date: Oct. 4, 2001

Signed: Gary S. Gray
Gary S. Gray

Date: _____

Signed: _____
Jerry Carson

Date: _____

Signed: _____
Kashi Javaherian

Date: _____

Signed: _____
Paul D. Rennert

Date: _____

Signed: _____
Sandra Silver

10027075-122001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Gary S. Gray et al.

Serial No.: 08/595,590

Filed: February 2, 1996

For: CTLA4-Immunoglobulin Fusion Proteins
Having Modified Effector Functions and Uses
Therefor

Attorney Docket No.: RPI-007

Group Art Unit: 1806

Examiner: Eyler, Y.

Assistant Commissioner for Patents
Washington, D.C. 20231

Certificate of First Class Mailing (37 CFR 1.8(a))

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on the date set forth below.

2-20-98
Date of Signature and of Mail Deposit

By:

Giulio A. DeConti, Jr.
Reg. No. 31,503

ASSOCIATE POWER OF ATTORNEY

Sir:

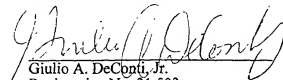
The undersigned attorney has the power of attorney in the subject application. He hereby grants an associate power to:

Megan E. Williams, Ph.D.
Registration No. P43,270
Lahive & Cockfield, LLP
28 State Street
Boston, MA 02109

10027075-122001

Please continue to forward all written and telephonic communications to Amy E.
Mandragouras at the address and telephone number listed below.

Respectfully submitted,


Giulio A. DeCinti, Jr.
Registration No. 31,503
Attorney for Applicants

LAHIVE & COCKFIELD, LLP
28 State Street
Boston, MA 02109
Tel. (617) 742-4214

Dated: February 20, 1998

10027075-122001